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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,082	08/07/2001	Lawrence J. Mamett	N-7362 RSM	1831
32885	7590	07/29/2005	EXAMINER	
STITES & HARBISON PLLC 424 CHURCH STREET SUITE 1800 NASHVILLE, TN 37219-2376			PAK, YONG D	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/924,082

Applicant(s)

MARNETT ET AL.

Examiner

Yong D. Pak

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 May 2005.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-54 is/are pending in the application.
- 4a) Of the above claim(s) 2, 5 and 22-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3, 4 and 6-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

The amendment filed on May 5, 2005, canceling claim 1, has been entered.

Claims 2-54 are pending. Claims 2, 5 and 22-54 are withdrawn. Claims 3-4 and 6-21 are under consideration.

Response to Arguments

Applicant's amendment and arguments filed on May 5, 2005, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-4, 6-8, 10-17 and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Yu et al.

Claims 3-4, 6-8, 10-17 and 19-21 are drawn to a method of detecting/measuring activity of COX-2 by detecting PGH₂-EA metabolites, wherein COX-2 activity is detected/measured via standard values/curves, various samples are derived from

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mammals, PGH₂-EA metabolites are detected via a mass chromatogram or the detection step includes an immunoassay.

Yu et al. (Reference BN: PTO-1449) teaches a method of detecting/measuring COX-2 in a sample derived from a mammalian cell by detecting/measuring a PGH₂-EA metabolites (Figures 2-6 and pages 21182). Arachidonyl ethanolamide (AEA), a precursor for PGH₂-EA metabolites is not a substrate for COX-1 and therefore, the method of Yu et al. only selectively detects COX-2 activity (page 21182, right column, page 21183, right column, page 21184, right column and page 21186, left column). Yu et al. generates a standard value and curve for determining COX-2 activity (Figure 1 and Table 1). Yu et al. detects/measure COX-2 activity by detecting PGH₂-EA metabolites via a mass chromatogram (Figures 3-5) and immunoassays (Figure 2 and Figure 6).

The metabolites detected in the method of Yu et al. encompasses the metabolites recited in claims 7 and 16 because the recited metabolites are naturally produced, enzymatically or nonenzymatically, from upon oxidation of AEA by COX-2. Yu et al. teaches that the metabolites of AA and AEA are identical (page 21185, left column and see KEGG – prostaglandin and leukotriene metabolism – form PTO-892).

Therefore, the teachings of Yu et al. anticipate claims 3-4, 6-8, 10-17 and 19-21.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that Yu et al. fail to disclose or suggest a method whereby direct detection of the claimed metabolite are indicative of an activity of a COX-2

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enzyme, i.e. step of detecting a COX-2 specific metabolite or detecting a metabolite of a COX-2 selective substrate to show COX-2 activity or whereby direct detection and quantification is indicative of an activity of a COX-2 enzyme. Examiner respectfully disagrees. The claims are drawn to a method of detecting/measuring activity of COX-2 by detecting PGH₂-EA metabolites. Yu et al. does teach a method of detecting/measuring activity of COX-2 by detecting PGH₂-EA metabolites. Since Yu et al. teaches that arachidonyl ethanolamide (AEA), a precursor for PGH₂-EA metabolites is not a substrate for COX-1, presence of PGH₂-EA metabolites "indicates the activity of the COX-2 enzyme" (as recited by the claim).

Applicants also argue that Yu et al. fails to disclose or suggest the downstream metabolites of the present invention, the significance of their presence and quantification. Examiner respectfully disagrees. As stated by applicants, Yu et al. disclose detecting/quantifying PGE₂ ethanolamide (page 21185). Since the claims do not recite the limitation that all the PGH₂-EA metabolites be detected/quantified, but selected from the group consisting of the recited PGH₂-EA metabolites, the reference of Yu et al. anticipates the claims.

Applicants also note that Yu et al. states "At the present time the physiological significance of the metabolism of AEA by COX-2 is not known.". The statement is moot since the claims are not drawn to any aspect of the physiological effects of AEA metabolism since PGH₂-EA metabolites are detected from a sample obtained from a mammal.

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Applicants also argue that the present invention provides significant advantages over the prior art, such as the ability to detect and/or quantify COX-2 directly in the patient. The argument is moot because the claims are not drawn to a method of detecting or quantifying COX-2 directly in the patient, but detecting PGH₂-EA metabolites from a sample obtained from a mammal.

Hence the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stichtenoth et al. and Yu et al.

Claims 9 and 18 are drawn to a method of detecting/measuring activity of COX-2 by detecting PGH₂-EA metabolites, wherein the sample is urine.

Stichtenoth et al. (form PTO-892) teaches the use of urine sample for assay of COX activity in general (abstract). From this reference, one of skilled in the art can conclude that urine can be used as a sample for detecting COX activity. Stichtenoth et al. teaches detecting/measuring COX-2 activity by detecting/measuring PGH₂ metabolites in urine samples (abstract).

The reference of Stichtenoth et al. does not teach a method of selectively detecting/measuring COX-2 activity by detecting PGH₂-EA metabolites in urine samples.

The reference of Yu et al. as it applies to claims 3-4, 6-8, 10-17 and 19-21, teaches a method of detecting/measuring COX-2 in a sample by detecting/measuring a PGH₂-EA metabolites (Figures 2-6 and pages 21182).

Combining the teachings of Stichtenoth et al. and Yu et al., it would have been obvious to one having ordinary skill in the art use urine samples to the method Yu et al. to detect COX-2 activity. One of ordinary skill in the art would have been motivated to selectively detect/measure COX-2 activity in I urine sample since the sameple can be easily obtained from a subject. One of ordinary skill in the art would have had a

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reasonable expectation of success since Stichtenoth et al. teaches the use of urine sample for measuring/detecting COX-activity and Yu et al. successfully teaches selective detection/measurement of COX-2 activity in a sample.

Therefore, the above references render claims 9 and 18 *prima facie* obvious to one of ordinary skill in the art.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that Stichtenoth et al. fails to remedy the deficiencies of Yu et al., which was discussed above, and since the cited references must, when combined, teach or suggest all of the claim limitations, the above combination does not present a *prima facie* case of obviousness. Since the reference of Yu et al. does anticipate claims 3-4, 6-8, 10-17 and 19-21 as discussed above, the combined teachings of Yu et al. and Stichtenoth et al. do teach or suggest all of the claim limitations.

Hence the rejection is maintained.

None of the claims are in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned

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are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner



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